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| 09/601,371 | 12/05/2000 | Tsukasa Seya | 49927 | 2244 |

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EDWARDS & ANGELL, LLP
P.O. BOX 55874
BOSTON, MA 02205

| EXAMINER | |
|---|---|
| MERTZ, PREMA MARIA | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1646 | |

DATE MAILED: 02/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/601,371 | SEYA ET AL. | |
| | Examiner | Art Unit | |
| | Prema M Mertz | 1646 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *24 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *15-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

***Election/Restrictions***

1. Applicant's election with traverse of Group II (claims 15-17) on 12/24/2003 is acknowledged. The traversal is on the ground(s) that the restriction is improper since the examiner has not shown that examination of all 5 Groups would entail a serious burden. This is not found persuasive because the searches for the five Groups would not overlap. Inventions I-V are independent and distinct, each from the other, because even though the methods are practiced with the same product the only feature in common in the instant inventions is "the method of treating diseases" with M161Ag, which does not constitute the special technical feature lacking from the prior art because this method can be used with a composition other than the instant products such as a mutein of IL-6 which binds to the IL-6 receptor and which acts as a receptor agonist. Furthermore, separate search terms would be required for searching the literature, eg. a search of the literature for an association of TNF-α with M161Ag would not necessarily reveal art for an association of IL-6 with M161Ag.

Having shown that these inventions are distinct for the reasons given above and have acquired a separate status in the art recognized divergent subject matter as defined by MPEP § 808.02, the Examiner has prima facie shown a serious burden of search (see MPEP § 803). Therefore, an initial requirement of restriction for examination purposes as indicated is proper.

The Groups as delineated in the restriction requirement on 11/26/2003 are patentably distinct one from the other such that each invention could, by itself, in principle, support its own separate patent (as shown by the arguments put forth in the written restriction requirement).

The requirement is still deemed proper and is therefore made FINAL.

Claims 15-17 will be examined only with respect to a method of treating diseases associated with TNF-α deficiency.

***Specification***

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. It is suggested that the title be amended to recite a method of treatment with M161Ag protein.

***Claim rejections-35 U.S.C. 112, first paragraph***

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3a. Claims 15-17 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure while being enabling for a method for increasing the level of TNF-α by purified peripheral blood monocytes in vitro by addition of M161Ag to the purified peripheral blood cells, does not reasonably provide enablement for a method of treatment of diseases caused by TNF-α deficiency by administering M161Ag. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The specification is non-enabling for the scope of the claimed method because the disclosure is not commensurate in scope with the claims for the breadth of the various kinds of diseases involving a deficiency of TNF-α that can be treated with M161Ag. The claims broadly encompass "any" caused by TNF-α deficiency. The claims encompass diseases ranging from leukemias to all types of solid tumors. However, the specification only enables a method of

increasing TNF-α in the conditioned medium of purified peripheral blood monocyte cells (see pg 7 and Figure 2). With respect to the other disparate diseases, the skilled artisan would have to undergo undue experimentation to determine if there is a therapeutically effective amount of M161Ag to be utilized for treating various diseases involving a deficiency of TNF-α. It would not be reasonable to expect the same amounts of M161Ag to work on the various types of aforementioned diseases because it is well known that results obtained with conditions such as solid tumors are certainly not representative of another disease, such as leukemias because the conditions are very dissimilar. Thus, it would require undue experimentation on the part of the skilled artisan to use the M161Ag in the method for treating leukemias, in the absence of sufficient information to predict the results with an adequate degree of certainty. Therefore, a method for treating the various TNF-α deficiency mediated diseases by use of M161Ag has not been enabled by the specification because the results obtained in Figure 2 are in vitro results and are not predictive of the full-scope of the claims. The recitation of "diseases caused by TNF-α deficiency" in the claims is not commensurate with the scope of the specification.

Furthermore, the specification is non-enabling for the method as claimed because to practice such a method would require knowledge of the route, duration and quantity of administration of the M161Ag protein to a subject for each of the diseases, and this information is not provided by the instant specification. The text on page 6 of the instant specification clearly fails to supply the guidance that would be needed by a routine practitioner. The instant specification has also failed to disclose how these parameters are to be determined, how a similar method was practiced in the art with a different agent or to provide even a single working example, prophetic or actual of the claimed method other than for administration to cells in vitro

as described on page 7, Figure 2. In the absence of this guidance, a practitioner would have to resort to a substantial amount of undue experimentation involving the variation in the amount and duration of administration of the proteins of the instant invention and in determining a suitable route of administration. The instant situation is directly analogous to that which was addressed in In re Colianni, 195 U.S.P.Q. 150, C.A.F.C., which held that a "disclosure that calls for application of 'sufficient' ultrasonic energy to practice claimed method of fusing bones but does not disclose what 'sufficient' dosage of ultrasonic energy might be or how those skilled in the art might select appropriate intensity, frequency, and duration, and contains no specific examples or embodiment by way of illustration of how claimed method is to be practiced does not meet requirements of 35 U.S.C. § 112 first paragraph".

The claims recite "a method of treatment of diseases caused by TNF-α deficiency". The instant specification is non-enabling for such a method in the absence of support to accomplish the purpose by administration of the M161Ag protein. The recitation of the term "TNF-α deficiency" in the claim indicates that the M161Ag causes alleviation of the TNF-α deficiency and the symptoms of the disease. Since the principle biological effects of administration of the protein would be to increase the ~~activity~~ circulating amount of this cytokine, the ability of the M161Ag to treat an unspecified disorder would not be an enabled paradigm. The M161Ag could not be administered with a predictable prognosis using the specification as guidance because the specification provides no examples nor is an enabling mechanism disclosed using the M161Ag commensurate with the scope of the claims. In the absence of such a disclosure a skilled artisan would be unable to practice the method embraced by the claims without undue experimentation. It would require undue experimentation for the ordinary artisan to determine how to use the M161Ag protein *in*

*vivo* in the treatment of diseases caused by TNF-α deficiency. Treatment of diseases caused by TNF-α deficiency with the M161Ag protein *in vivo* would have not been believable by one of ordinary skill in the art at the time of filing of the instant application.

Furthermore, in The Cytokine Facts Book (1994), Robin Callard and Andy Gearing. Academic Press Inc. San Diego, CA, the functions of TNF-α range from a mediator of inflammatory and immune functions to its cytotoxicity for many transformed cells (page 241, second para). However, the instant specification (page 4, lines 6-11) discloses that M161Ag induces cells to apoptotic death and suppressed disease states caused by immune activation such as allergy. Based solely on Applicants specification, it would be clearly impossible for one skilled in the art to use the M161Ag protein in a method of treatment of diseases caused by TNF-α deficiency as claimed.

In view of the above discussion, the claims are not commensurate in scope with the specification but are directed to products that are broader than the supporting disclosure.

***Claim rejections-35 U.S.C. 112, second paragraph***

4. Claims 15-17 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15 is vague and confusing. It is suggested that the claims be amended to recite the specific method being claimed. i.e. the TNF-α deficiency for which the M161Ag protein is being administered. The metes and bounds of the term "diseases" is unclear because it can range from leukemias to allergies to infections. It is suggested that the claims be re-written and presented as

separate claims for a method of treatment of specific diseases caused by the various cytokine deficiencies.

Claims 16-17 are rejected as vague & indefinite insofar as they depend on claim 15 for its limitations.

***Claim rejections-35 U.S.C. 103***

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Matsumoto Misako (1997).

Misako describes a new membranous protein M161Ag, the amino acid sequence of the M161Ag protein and suggests that the protein has actions on promotion of the clearance of cancer cells, especially a human myelocytic leukemic cell and is also useful as a therapeutic agent for leukemia. However, Misako never administered the M161Ag protein to human leukemic cells to show the ability of M161Ag as a therapeutic agent.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the instant invention was made to administer the M161Ag protein to human myelocytic leukemic cells as disclosed by Misako and obtain the desirable results as suggested by Misako. To have administered the M161Ag protein would have been *prima facie* obvious to an artisan in light of the Misako publication, especially since the instant claims fail to recite a specific disease to be treated. Furthermore, it would have been obvious to one of ordinary skill in the art at the time that the invention was made that the M161Ag protein being a membranous protein was acylated with fatty acid at an N-terminal position.

***Conclusion***

No claim is allowed.

***Advisory Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (703) 308-4229. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564.

Official papers filed by fax should be directed to (703) 305-3014 or (703 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 746-5300.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [yvonne.eyler@uspto.gov].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark Office on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Prema Mertz

Prema Mertz Ph.D.
Primary Examiner
Art Unit 1646
January 7, 2004